Joint Pathology Center
Veterinary Pathology Services

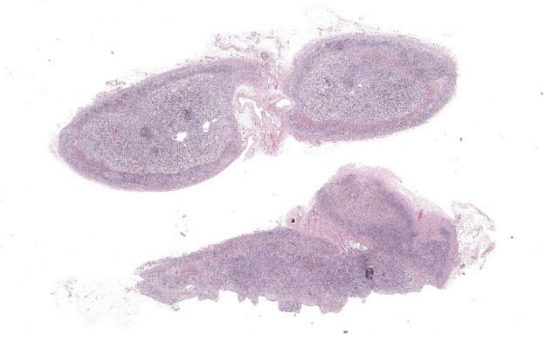
WEDNESDAY SLIDE CONFERENCE 2026-2027

Conference #2 — 26 August 2026

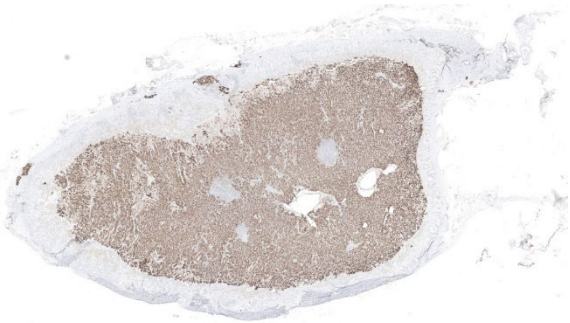
CASE I:

Signalment:
4-year-old male neutered Labradoodle (*Canis lupus familiaris*)

History:
This patient presented to the emergency department for 2 days of vomiting and diarrhea with a historical seizure following weakness at home. Clinical examination revealed that the dog was obtunded, weak, in shock and hypoglycemic. He was treated for cerebral edema without response and required up to 10% dextrose to maintain normoglycemia. Bloodwork was suggestive of sepsis, but the abdominal ultrasound was not consistent with septic peritonitis and the fluid was too scant to obtain. The patient arrested before an echocardiogram could be performed and before blood cultures, urine cultures and ACTH stimulation test results returned. The tentative clinical diagnosis was sepsis of unknown source.



1-1. Adrenal gland, dog: Two sections of adrenal gland are submitted for examination. The cortex is markedly reduced in thickness with a cortex:medulla ratio of 1:5. (HE, 10X).

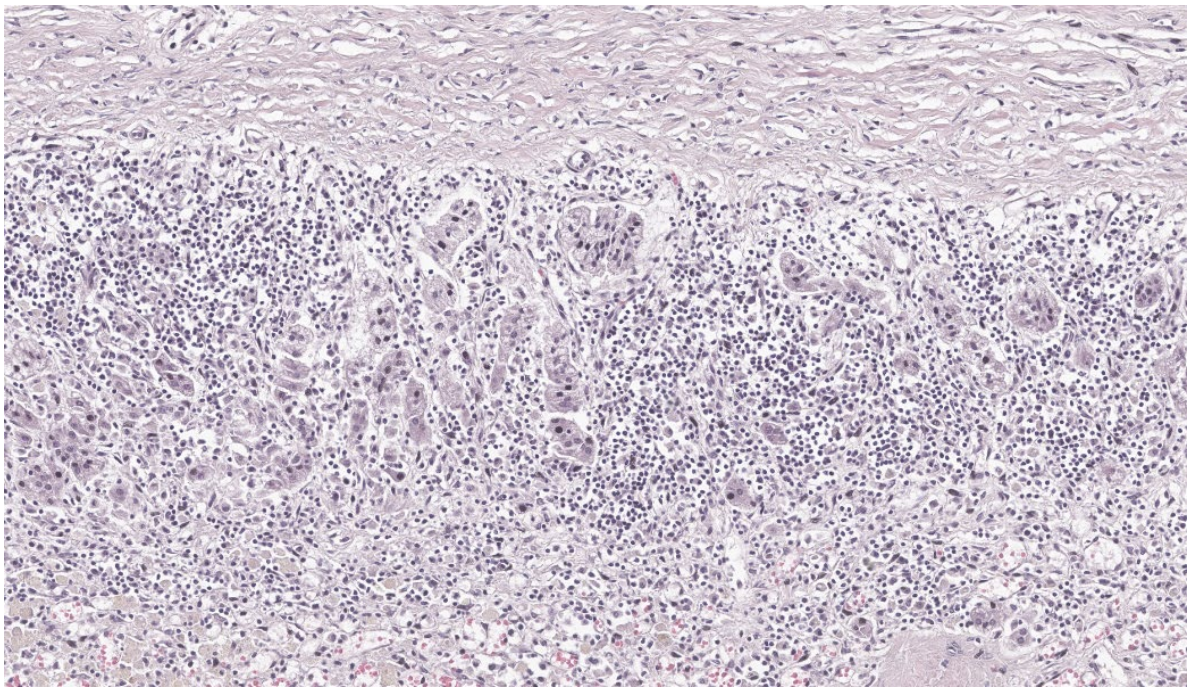


1-2. Adrenal gland, dog: A chromogranin A immunomarker (which stains medullary cells) better demonstrates the corresponding thicknesses of the cortex and medulla.) (anti-chromagranin A, Two sections of adrenal gland are submitted for examination. The cortex is markedly reduced in thickness with a cortex:medulla ratio of 1-5. (HE, 30X).

Gross Pathology:
The adrenal glands are reduced in size bilaterally and measure 1.5 x 0.4 x 0.5 cm on the right and 1.8 x 0.5 x 0.5 cm on the left. The adrenal cortices appear bilaterally attenuated (approximate cortex to medullary ratio of 1:5). The thyroid/parathyroid and pituitary glands are grossly within normal limits.

Laboratory Results:
Chemistry panel:

Glucose initially too low to read on in-house panel,



1-3. Adrenal gland, dog: Higher magnification of the inflamed and atrophic adrenal cortex. There is loss of the normal architecture with remnant aggregates of cortical cells infiltrated by numerous lymphocytes, plasma cells, and histiocytes and an expanded stroma. (HE, 247X).

Sodium is 146 mmol/L (reference 142-152 mmol/L),

Potassium is 4.4 mmol/L (reference range 4.0-5.4 mmol/L),

Sodium: potassium ratio is 33 (reference range 28-37),

Cholesterol: 105 mg/dL (L) (reference range 131-345 mg/dL)

Albumin: 2.4 g/dL (L) (reference range 2.7-3.9 g/dL)

Cortisol levels are 0.6 µg/dL (L) (reference range 2.0-6.0 µg/dL)

CBC:

White blood cells are 2.5 K/µL (L) (reference range 4.9-17.6 K/µL),

Neutrophils are 0.1K/µL (L) (reference range 2.94-12.67 K/µL),

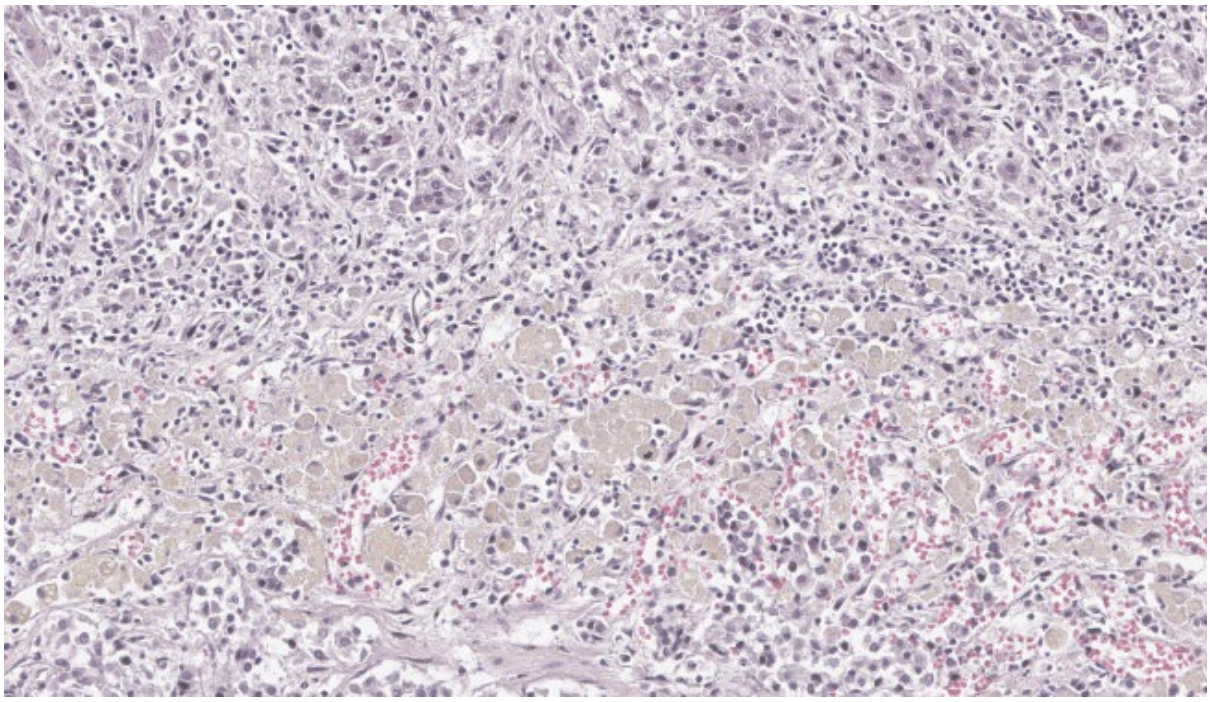
Lymphocytes are 2.15 K/µL (reference range 1.06-4.95 K/µL,

Monocytes are 0.05 K/µL (L) (reference range 0.13-1.15 K/µL)

Eosinophils are 0.2 K/µL (reference range 0.07-1.49 K/µL),

Microscopic Description:

Two adrenal glands (one section of each) are examined. In each section, the cortex is severely attenuated, with a reduced cortex to medullary ratio (approximately 1:5). The zona glomerulosa can be visualized, however, the zonae fasciculata and reticularis are severely atrophied to absent with stromal collapse and rare remaining cortical cells. These remaining cells are interspersed by inflammation and exhibit cytoplasmic vacuolation. The deeper layers of the cortex are largely replaced by inflammatory cells, including macrophages, lymphocytes and plasma cells, intermixed with fibrous connective tissue (fibrosis). Fibrous tissue is highlighted with a Masson's trichrome stain. Macrophages contain abundant, yellow to gold and brown granular pigment

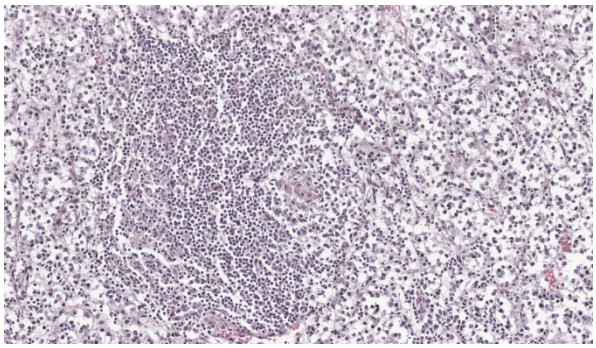


1-4. Adrenal gland, dog: There is a band of macrophages with abundant golden brown cytoplasmic pigment at the corticomedullary junction. (HE, 318X)

(presumed lipofuscin, hemosiderin). Small amounts of hemorrhage are intermixed with the inflammatory cells of the adrenal cortex. The medullary portion of the adrenal gland is intact, recognizable by cells of a neuroendocrine phenotype, containing a granular, amphophilic to basophilic, often vacuolated cytoplasm with separation into small packets by a fine fibrovascular stroma. Small amounts of scattered inflammation extend into the medulla, including lymphocytes, plasma cells and macrophages.

Contributor's Morphologic Diagnosis:
Adrenal glands: Adrenalitis, histiocytic, lymphoplasmacytic, severe, with regional cortical atrophy, collapse and loss (zonae fasciculata and reticularis), lipofuscin and hemosiderin accumulation (consistent with idiopathic adrenocortical atrophy, primary atypical adrenal insufficiency, hypoadrenocorticism / Addison's disease)

Contributor's Comment:
Nonsuppurative adrenalitis with severe atrophy and loss of the adrenal cortex correlates with the gross findings of adrenal cortical attenuation. The zonae fasciculata and reticularis were primarily affected and were unable to be visualized within the section. The outer zona glomerulosa was also inflamed, however, remnant tissue was present, which may explain the atypical presentation of this patient (lack of electrolyte abnormalities on bloodwork). Approximately 85%-90% of the adrenal cortex must be nonfunctional before clinical signs can be observed.3,9 In this case, sodium and potassium levels were within normal limits on the chemistry panel. Concurrent hyponatremia and hyperkalemia with a sodium:potassium ratio of greater than 23:1 can be used for clinical identification of hypoadrenocorticism.[2,3,9] Similar electrolyte changes can occur with gastrointestinal disease (including parasitism), renal and hepatic disease, congestive heart failure, pleural effusion and severe metabolic or respiratory acidosis.[2]



1-5. Adrenal gland, dog: There are aggregates of lymphocytes with fewer plasma cells and macrophages with in the medulla as well. (HE, 342X)

Primary adrenal insufficiency, (hypoadrenocorticism or Addison's disease) is characterized by reduced mineralocorticoid and/or glucocorticoid production by the adrenal glands.[2] Secondary and tertiary (or central) hypoadrenocorticism are associated with abnormalities in the pituitary gland which produces adrenocorticotropic hormone (ACTH) or the hypothalamus which produces corticotropic releasing hormone (CRH).[2] Secondary hypoadrenocorticism can occur with pituitary destruction caused by neoplasia, inflammation or head trauma.[3] Tertiary hypoadrenocorticism has not been definitively diagnosed in dogs.[2] Hypoadrenocorticism in dogs has an estimated prevalence between 0.06 and 0.3%.[2] Breed related predispositions have been reported, including a strong heritable component in standard poodles as well as Portuguese water dogs, Nova Scotia duck tolling retrievers, soft coated wheaten terriers and bearded collies.[2,3,9] Females are at increased risk (1.9-2.6 times greater), however, this has not been identified in all studies, which may reflect different breed-genetic risk factors. The reported median age is 3-4 years, however, dogs with glucocorticoid deficiency alone (the "atypical" form) are commonly older (6-8 years old).[2,4,8] Affected dogs usually have vague, non-specific clinical signs, and hypoadrenocorticism has been referred to as "the great pretender".[2,3] Clinical characteristics that can raise suspicion for hypoadrenocorticism include waxing and waning gastrointestinal signs that respond rapidly to fluid or glucocorticoid therapy and are exacerbated by stress.[2] Patients with the atypical form are reported to have a longer duration of clinical signs, likely because this form is more challenging to identify.[4,8]

The baseline cortisol level of this patient was below the reference range and the ACTH stimulation test results were not available. This patient was not receiving any medication and other than a historical "sensitive stomach", was reported to have been clinically normal prior to the onset of vomiting and seizures. "Typical" primary hypoadrenocorticism encompasses glucocorticoid deficiency accompanied by mineralocorticoid deficiency, whereas "atypical" is loosely described as glucocorticoid deficiency in the absence of mineralocorticoid deficiency.[2] The atypical form represents a minority of cases (approximately 5-10%).[3,9] One study found that dogs with the "atypical" form have decreased basal and ACTH stimulated aldosterone levels, suggesting mineralocorticoid deficiency despite the lack of electrolyte abnormalities.[9] A subset of dogs without electrolyte abnormalities will subsequently develop them within a year of diagnosis.[9] Standardized nomenclature for these terms has not been established. The Agreeing Language in Veterinary Endocrinology (ALIVE) project suggests referring to "typical" as hyponatremic and/or hyperkalemic primary hypoadrenocorticism and "atypical" as eunatremic, eukalemic primary hypoadrenocorticism.[2] In order to avoid confusion, herin, "atypical" glucocorticoid deficient hypoadrenocorticism will be referred to as GDH and "typical" mineralocorticoid-glucocorticoid deficient hypoadrenocorticism as MGDH.[8]

Acute adrenocortical insufficiency (Addisonian crisis) can be a life-threatening condition that clinically presents as shock, dehydration and metabolic derangements (the latter with MGDH).[2,4,6] Hypotension can be attributed to hypovolemia, poor vascular tone and lack of compensatory tachycardia. Mortality can occur with hyperkalemia, hyponatremia, dehydration and hypovolemic shock.[2] Possible complications include gastrointestinal ulceration, DIC, sepsis caused by bacterial translocation from the gastrointestinal tract, and aspiration pneumonia (due to megaesophagus).[2,6] Collapse in GDH has been reported with hypoglycemia, sepsis and GI hemorrhage.[4] The mainstays of treatment for hypoadrenocorticism include fluid resuscitation, glucocorticoid administration, correcting hypoglycemia and electrolyte abnormalities, if present.[4,6,9] A recent study found that intravenous CRI of hydrocortisone as a treatment for acute Addisonian crisis is well-tolerated and safe but had no clear benefit when compared with traditional glucocorticoid replacement.[6] With appropriate treatment and recovery following a crisis and lifelong administration of medical therapy, the prognosis is excellent for normal life expectancy.[6,9]

Definitive diagnosis of hypoadrenocorticism requires histologic evaluation of the adrenal glands and correlation with clinical parameters. The adrenal cortex has three functional zones. The outer zona glomerulosa (25% of the cortex) produces mineralocorticoids (aldosterone) and supplies precursor cells for the inner 2 layers.[2,3,9] The middle zona fasciculata (60% of the cortex) produces glucocorticoids, and the inner zona reticularis (15% of the cortex) produces androgens.[2,9] Aldosterone regulates water, acid-base and electrolyte homeostasis via increasing sodium absorption and potassium secretion.[2] Aldosterone mainly targets the kidney and is the most important hormone affecting renal potassium excretion.[3] Immune mediated destruction is the most common cause of primary hypoadrenocorticism in dogs and is suspected in this case. Uncommon causes of adrenal gland destruction and hypoadrenocorticism include inflammatory or neoplastic diseases, amyloid deposition, infarcts and drug administration (e.g., mitotane, trilostane, sudden withdrawal of steroids). Any inflammatory, neoplastic, vascular, infectious, traumatic or developmental process affecting the hypophysis can result in secondary hypoadrenocorticism.[1,2,9]

Several immune response genes have been identified for determining susceptibility to Addison's disease in humans. Supporting evidence of an autoimmune pathogenesis was demonstrated in dogs with hypoadrenocorticism, encompassing circulating autoantibodies against steroid synthesis enzyme 21 hydroxylase and p450 side chain-cleavage enzyme.[1] Overlap of autoimmune diseases is common, and approximately 50% of humans with Addison's disease have other autoimmune diseases.[1] Dogs and humans with hypoadrenocorticism may have concurrent hypothyroidism, diabetes mellitus or hypoparathyroidism.[1,9] A genetic component to canine hypoadrenocorticism is suspected, given the strong breed associations in epidemiologic studies.[1,2] Molecular genetic studies have found that genes and signaling pathways similar to those implicated in humans may be associated with canine hypoadrenocorticism. Genetic variation in the genes encoding MHC class II proteins (which plays an important role in the adaptive immune system) have been associated with autoimmune diseases in multiple species.[1] Immune response genes which may be important for increased susceptibility to hypoadrenocorticism in dogs in-

clude dog leukocyte antigen (DLA) and cytotoxic T-lymphocyte associated protein 4 (CTLA4).[1,5] A genome wide microsatellite analysis in Portuguese water dogs showed a strong association with the DLA region of chromosome 12 and a marker close to CTLA4 on chromosome 37.[1] Despite the clear association with genetic factors, canine hypoadrenocorticism is most likely a complex genetic disorder.[1] In humans with primary adrenal insufficiency, many genetic causes have been identified and include disorders of steroidogenesis, defects in cholesterol biochemistry, peroxisomal defects, mitochondrial disorders, abnormal adrenal development, ACTH resistance and autoimmune polyglandular syndromes.[7]

Cortisol has many roles, including regulating circulating glucose concentrations, enhancing urinary calcium excretion and reducing absorption, maintaining the normal function of the intestinal mucosa, sustaining myocardial performance and increasing cardiac output, facilitating arteriolar constriction, helping to maintain normal blood pressure and volume, stimulating production of erythrocytes, release of platelets and neutrophils from the bone marrow and suppressing lymphocyte proliferation.[2] Basal cortisol levels less than 55 nmol/L is highly sensitive for diagnosis of hypoadrenocorticism, thus is a useful screening test. The cortisol levels in this case were 0.6 ug/dL or 17 nmol/L, well under the cutoff of 55 nmol/L. The ACTH stimulation test is the test of choice for diagnosis of hypoadrenocorticism.[2] Hypoglycemia was also present in the submitted case, which is a common abnormality with hypoadrenocorticism due to glucocorticoid insufficiency. In one review, hypoglycemia was found in 31% of GDH cases, presumably due to decreased hepatic gluconeogenesis and increased peripheral sensitivity to insulin.[2] Clinical signs referable to hypoglycemia included profound weakness and seizures.[2]

In one study comparing GDH and MGDH, hypocholesterolemia and hypoalbuminemia were more commonly observed in the GDH group.[8] Hypocholesterolemia may be attributable to reduced gastrointestinal lipid absorption, reduced mobilization of fatty acids due to low cortisol or increased utilization from high ACTH concentrations.[8] Interestingly, hypocholesterolemia and hypoalbuminemia were also observed in this case. Hypercalcemia is observed in approximately 30% of dogs with hypoadrenocorticism and was not observed in this case.[9] A stress leukogram (neutrophilia, lymphopenia, monocytosis and eosinopenia) occurs with cortisol release. In hypoadrenocorticism, a stress leukogram may not be present in the face of systemic illness. In addition, a reverse stress leukogram can be observed in cases of hypoadrenocorticism, which comprises eosinophilia and lymphocytosis.[2,8,9] Reduced cortisol increases bone marrow eosinophil production and decreases eosinophil migration into tissues, resulting in increased eosinophil levels in the blood. Cortisol can also reduce the numbers of circulating lymphocytes, thus cortisol deficiency results in increased numbers of lymphocytes.[2] However, these changes are not present in a significant percentage of cases and have limited diagnostic value.[2] In this case, the components of a reverse stress leukogram were not present, however, neutrophils and monocytes were below the reference ranges and sepsis was suspected, but could not be confirmed.

Contributing Institution:
Schwarzman Animal Medical Center, Department of Anatomic Pathology,
www.amcny.org

JPC Diagnosis:
Adrenal gland: Adrenalitis, lymphoplasmacytic and histiocytic, chronic, diffuse, marked, with severe pancortical atrophy and loss.

JPC Comment:
This week's moderator was LTC Daniel Bland, JPC Class of '23, a previous WSC coordinator, POLA '25 course director, and the current Director of Pathology at the Walter Reed Army Institute of Research.

The contributor has provided their typical outstanding review of their submitted case, this time of Addison's disease in dogs (and many details of the disease in humans). As the reviews submitted by the staff of the Animal Medical Center are always thorough, it remains to the JPC to proceed in a totally different direction. So, let's briefly review hypoadrenocorticism in the cat.

Hypoadrenocorticism is considered rare in cats, although the non-specific and often intermittent clinical signs likely have led to underdiagnosis. Predisposing factors appear to be both primary and secondary in this species. Primary diseases result in the destruction of the adrenal cortex and include both adrenal cortical tumors and metastatic neoplasia, such as lymphoma; immune-mediated targeted destruction of the adrenal cortex; and congenital disease has been suggested in cases seen in cats less than 12 months of age. Secondary causes include tumors of the pituitary gland resulting in diminished ACTH secretion, as well as the sudden withdrawal of corticosteroids following their long-term administration.[10] Feline hyperadrenocorticism is associated with waxing and waning clinical signs, with non-specific signs such as lethargy, anorexia, weakness, and polyuria/polydipsia predominating. Laboratory findings in affected animals include hypochloremia, hyponatremia, and hypokalemia, with azotemia and hyperphosphatemia typically accompanying the condition in dehydrated animals. Interestingly, in this species, a study evaluating decreased sodium-potassium ratios in affected cats found that this ratio did not contribute to the diagnosis in any cases, and decreased Na: K ratios were seen in a range of other diseases and several types of effusions.[11] As in the dog, baseline cortisol levels and ACTH stimulation are paramount in the diagnosis of feline hypoadrenocorticism, and plasma ACTH is useful in identifying pituitary-associated diseases, such as neoplasia.[10]

Hypoadrenocorticism is a rare condition in other domestic species and has been identified in horses and ferrets. Rapid withdrawal of long-term steroids has been documented as a cause in these species (as would be expected in any species). In foals, it has been associated with sepsis, and in adult horses, ischemic injury as seen in endotoxic shock, associated with the Waterhouse-Friedrichsen-like syndrome.[13] In the ferret, it is typically iatrogenic, as long-term corticosteroid therapy is often employed in non-surgical patients with insulinoma to boost glucose levels, and occasionally when bilateral adrenalectomy is performed to treat adrenal neoplasia. In these cases, rapid withdrawal of glucocorticoids in hypoglycemic animals or mineralocorticoid replacement (given monthly in bilaterally adrenalectomized ferrets) may result in Addisonian crises. (BH Williams, personal communication).

References:
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8. Thompson AL, Scott-Moncrieff JC, Anderson JD. Comparison of classic hypoadrenocorticism with glucocorticoid-deficient hypoadrenocorticism in dogs: 46 cases (1985-2005). J Am Vet Med Assoc. 2007 Apr 15;230(8):1190-4.

9. Van Lanen K, Sande A. Canine hypoadrenocorticism: pathogenesis, diagnosis, and treatment. Top Companion Anim Med. 2014 Dec;29(4):88-95.

10. Glebocka MJ, Boag A. Hypoadrenocorticism in cats: a 40-year update. J Feline Med Surg. 2024 Sep;26(9):1098612X241248381.

11. Bell R, Mellor DJ, Ramsey I, Knottenbelt C. Decreased sodium: potassium ratios in cats: 49 cases. Vet Clin Pathol. 2005 Jun;34(2):110-4.

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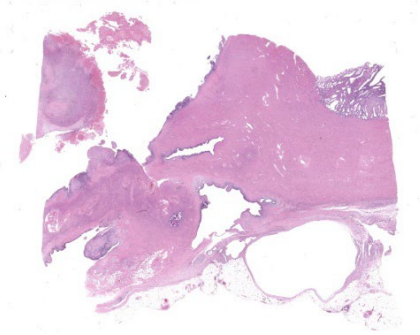
CASE II:

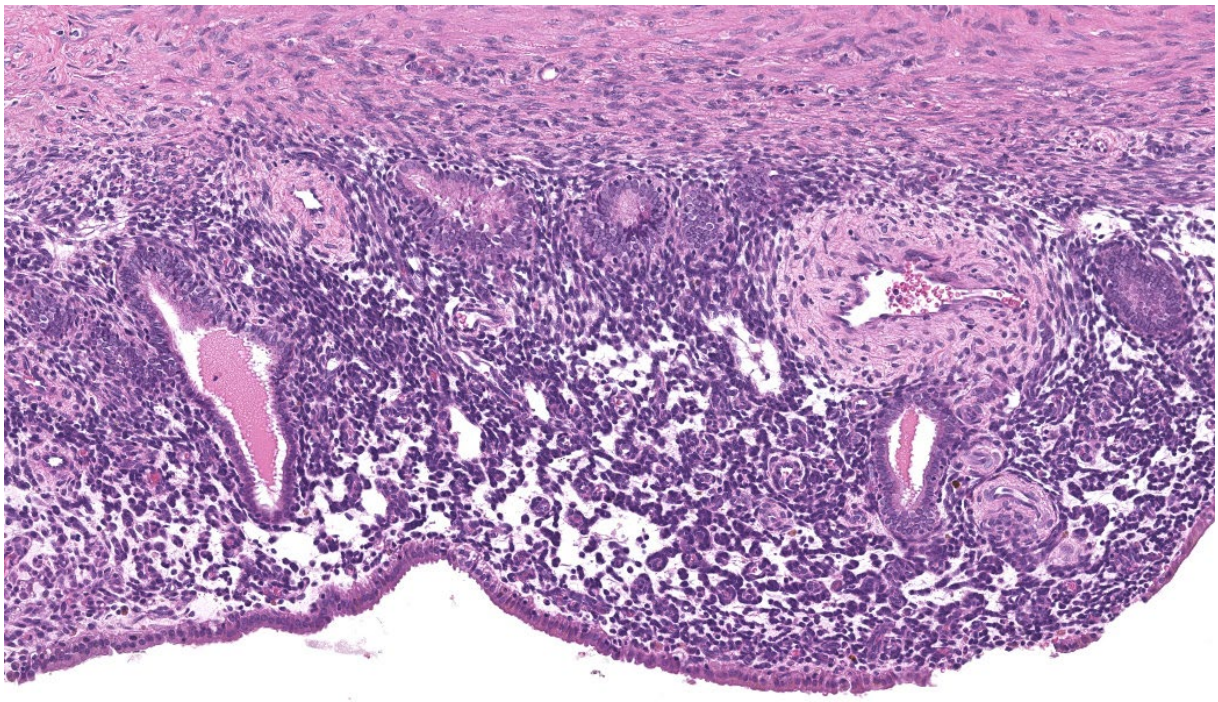
Signalment:
12 year old female Cynomolgus macaque (*Macaca fascicularis*)

History:
This 12-year old female cynomolgus macaque had a caudal abdominal mass discovered on annual physical examination; endometriosis was suspected. The NHP (nonhuman primate) was treated on 17 July 20 with medroxyprogesterone acetate. The mass reduced in size but did not resolve and the clinicians elected to euthanize the animal.

Gross Pathology:
Within the abdomen there were many adhesions between the urinary bladder, uterus, ovaries and descending colon, and red serosal nodules on the surface of the urinary bladder.



2-1. Uterus and mesometrium, cynomolgus macaque: The wall of the uterus (endometrium at upper right) is infiltrated by endometrial glands and peripherally, stroma. Similar glands extend along the serosa and infiltrate the adhered mesometrium (a 7cm cystic gland is present at lower right).



2-2. Uterus, cynomolgus macaque: The morphology of the infiltrating endometrial glands and surrounding stroma is best visualized along the serosa. (HE, 284X)

Additionally, there were also adhesions between the omentum, mesentery of the large intestine and the uterus/mesometrium. There were multiple thin walled, brown cysts that ranged in size from 3-6 mm on and around the adhesed uterine serosa and nodular thickening in the wall and serosal surface of the uterus. Both ovaries appeared enlarged, up to 2.5 cm, including the presence of thin wall cysts that contained brown gelatinous debris.

Microscopic Description:

Uterus and mesometrium: Expanding and disrupting the serosal surface of the uterus and adjacent mesometrium is a vigorous endometrial lining with a variably thick underlying stroma, occasionally forming tortuous uterine glands, and large 2-6 mm fibrovascular polypoid nodules that blend inconspicuously with the incongruous uterine stroma. The fibrovascular nodules contain dense whorls of convoluted, hyperplastic and occasionally vacuolated spindle cells, variable amounts of dense sclerotic collagen and low to moderate numbers of macrophages and multinucleate giant cells which often contain either brown pigment (hemosiderin), pale eosinophilic to amphophilic material (secretory product) or clear vacuoles (lipid). There is a moderate amount of a coagulum containing necrotic debris, eosinophilic secretory product and hemorrhage ("chocolate cyst" contents) adhering to the outer surface of said nodules. There are small amounts of hemorrhage and low numbers of lymphocytes underlying and/or sporadically within the disarranged endometrial epithelium. There is a 7 mm empty, thin walled cyst on the surface of the uterine serosa lined by a flattened, attenuated epithelium and surrounded by fibrous tissue containing low numbers of the aforementioned macrophages and multinucleated giant cells. Rarely within the myometrium there are uterine glands surrounded by low numbers of lymphocytes. The

endometrium is mildly hyperplastic containing enlarged, tortuous uterine glands on a thickened stroma.

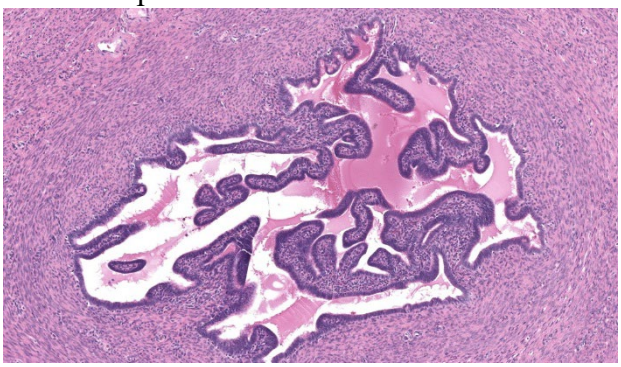
Contributor's Morphologic Diagnoses:
Uterus and mesometrium:

1. Endometriosis, cynomolgus macaque (*Macaca fascicularis*), nonhuman primate.

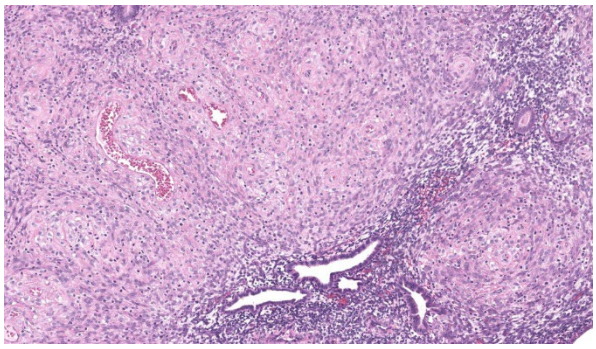
2. Uterus, serosa: Cyst, focal.

3. Uterus, myometrium: Adenomyosis, multifocal, minimal.

Contributor's Comment:
Endometriosis is the presence of "ectopic" endometrial tissue at a site outside of the uterus and it is the most common reproductive disorder in menstruating Old World primates. The prevalence of endometriosis increases with increasing age in rhesus macaques and there is evidence that endometriosis may have a genetic basis in humans and rhesus macaques.[8] Besides age and familial association, other risk factors include previous hysterotomy and long term estrogen treatment. Dioxin exposure has also been implicated in the development of endometriosis and exposure to dioxin has been shown to facilitate the growth of endometrial explants.[3]



2-3. Uterus, cynomolgus macaque: Endometrial glands and stroma invade the smooth muscle wall of the uterus (adenomyosis). (HE, 190X)



2-4. Uterus, cynomolgus macaque: The stroma surrounding some infiltrating glands is swollen by abundant vacuolated cytoplasm (decidualization). (HE, 190X)

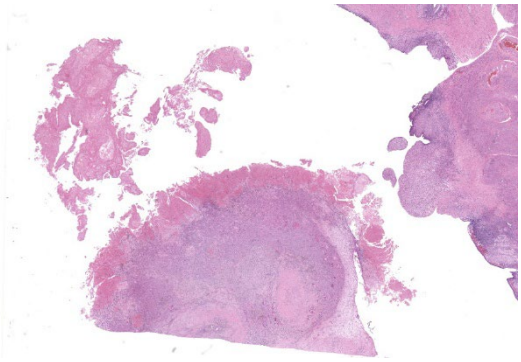
While the precise etiology of endometriosis is unclear, one of the most widely accepted theories includes retrograde menstruation of endometrial material into the peritoneal cavity.[5] A second theory includes the development of endometriosis from metaplasia of cells lining serosal surfaces, including the abdominal and thoracic structures. Finally, a third theory referred to as the induction theory proposes retrograde menstruation produces substances that induce metaplasia of peritoneal serosa.[1]

Clinically, presenting signs vary depending on the location of the endometriosis tissue implant. The disease may often be clinically silent and diagnosed as an incidental finding at necropsy. In symptomatic cases, animals may exhibit apparent abdominal discomfort or prostration. Other clinical signs that have been reported include: cyclical anorexia, depression, irregular menses and possibly constipation lasting several days. On physical examination, abdominal masses may be palpated.[3]

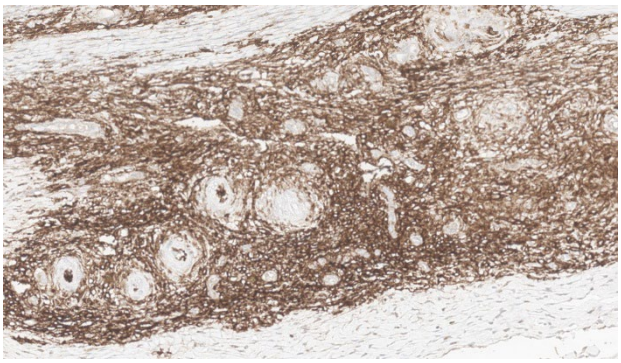
The condition can be quite heterogeneous, varying in degree and level of invasiveness between patients. While it is most commonly found in the pelvic region, it may be located anywhere throughout the abdomen and rarely

in extra-abdominal locations such as the thoracic cavity.[1] At necropsy, abdominal distention may be evident with the presence of endometrial explants and discrete cysts. Secondary lesions of the urinary tract such as hydroureter or hydronephrosis may occur due to fibrosis and adhesions.[6] In this case, the endometriosis appeared to be quite invasive with the formation of exophytic masses as well as development of invasive islands of endometrial stroma and glands and the formation of numerous cysts and reactive fibrosis. This case also had endometrial glands within the myometrium (adenomyosis) which is also considered to be part of endometriosis.[4] Decidualization of foci of endometriosis in response to endogenous or exogenous progestins has also been reported in multiple nonhuman primate species but was not observed in this case.[2]

Spontaneous endometriosis in non-human primates has been studied as an animal model for the disease in women. Both cynomolgus macaques and baboons have similar menstrual cycles as women and develop endometriosis spontaneously. Laparoscopic or open surgery has been used to diagnose and monitor the condition in non-human primates. Levels of



2-5. Uterus, cynomolgus macaque: Another section, primarily consisting of decidualized endometrial stroma surrounded by a fibrous wall, has large areas of necrosis, inflammation, and hemorrhage, consistent with a "chocolate cyst".



2-6. Uterus, cynomolgus macaque: CD10 is an excellent marker for endometrial stroma. Here in the serosa, it highlights the stroma of endometriosis lesions, but does not stain the glandular epithelium. (HE, 219X)

CA125 had also been measured in cynomolgus macaques with endometriosis and elevated levels were found to correlate with the presence of chocolate cysts.[7]

Contributing Institution:
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Fort Detrick, MD 21702
https://www.usamriid.army.mil/

JPC Diagnoses:
1. Uterus, mesometrium: Endometriosis with multifocal decidualization.
2. Uterus: Endometrial hyperplasia, chronic, diffuse, moderate with adenomyosis and multifocal decidualization.

JPC Comment:
The contributor has reviewed the basics of endometriosis in humans and non-human primates, but because maintaining non-human primates for laboratory research and drug development is difficult, various smaller animal models, particularly rodents, have received significant focus in the last decade. Researchers have developed a variety of rodent (primarily mouse) models. The intraperitoneal injection, laparoscopic implantation, or peritoneal suturing of uterine endometrial tissue

from donor mice creates autologous (homologous) mouse models. Heterologous models are created by injecting human endometrial tissue into the peritoneal cavity of immune-deficient mice. Other mouse models include transgenic and knockout mice, which allow determination of the effects of particular hormones or cytokines on disease progression, and mouse models expressing green fluorescent proteins that help monitor disease progression in immune-deficient mice in a less invasive manner.[9,10]

There are also numerous advances in the etiopathogenesis of the human disease – too many to recount here; one interesting development is the discovery of the roles of microRNAs (miRNAs) in the pathogenesis of endometriosis.[11] MicroRNAs are small noncoding RNA fragments consisting of 20 or 20 base pairs that do not produce protein, but regulate gene expression. Researchers have identified these miRNAs in both human patients and baboons with endometriosis. Upregulated MiR-29c has been shown to increase progesterone resistance, contributing to endometriosis-associated infertility. MiR-451 has been shown to downregulate apoptosis and enhance proliferation and invasion of endometriotic lesions. MiR-210 has been shown to enhance cell proliferation and migration in ectopic endometriosis lesions, and MiR-15a-5p, when suppressed, is involved in angiogenesis. This is only one facet of the fascinating research into endometriosis today.

While we agree with the contributor's diagnosis in this case, we found areas of decidualization in the submitted sections. (It is not unusual that sections that the contributor evaluated are not necessarily those submitted for a conference.) Atkins et al. (2016) documented decidualization of endometrial lesions.[2] In the normal animal, decidualization of endometrial stromal cells is a normal progesterone-driven phenomenon that transforms endometrial stromal cells in order to support early embryonic development and ultimately help to maintain pregnancy. In primates during pregnancy, this tissue is also commonly found in ectopic locations, primarily on the exterior of the ovary and uterine tube, but may explant to other, predominantly intra-abdominal, locations.[2]

A similar process will occur in primates with endometriosis. In primates with endometriosis, endometrial stromal cells surrounding some or all of the endometrial explants demonstrate a characteristic morphologic change with marked increase in lightly eosinophilic cytoplasm. These foci may be infiltrated by endometrial granular leukocytes (a form of gamma/delta T-cells) which possess numerous cytoplasmic red granules (seen in low numbers in decidualized foci in this slide).[2] In this case, decidualized tissue is also strongly positive for CD10 and vimentin.[2] (Both of these immunomarkers stain both normal and neoplastic endometrial stroma, so they are not specific for the decidualization process, but merely identify these cells as endometrial stroma.

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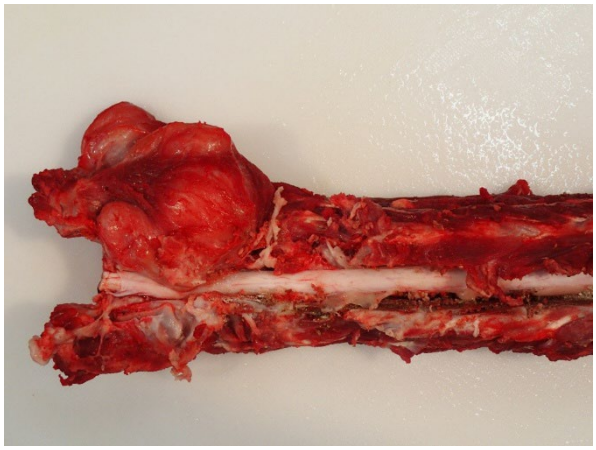
CASE III:

Signalment:
A 5-month-old female Dorset lamb

History:
The lamb showed progressive development of ataxia and incoordination. The owner noticed a small nodule behind the ear at the site of Gudair® (ovine Johne's disease) vaccination. The owner's farm had a previous history of copper deficiency in lambs

Gross Pathology:
A pale tan to white irregular fleshy mass containing multiple foci of caseous material extended from the right dorsal cervical musculature into spinal canal at the C1–C2 intervertebral space. The mass compressed the underlying spinal cord. Gross examination was otherwise unremarkable.



3-1. Cervical spine, sheep. A pale tan to white irregular fleshy mass extended into the cervical spinal canal at the level of C1-C2. (*Photo courtesy of:* Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, https://www.u-vet.com.au/).

Laboratory Results:
Serum copper was 12.7 µmol/L (Reference 7.5- 20 µmol/L) and liver copper level was 2.42 µmol/L (reference 0.23 – 3.67 µmol/L).

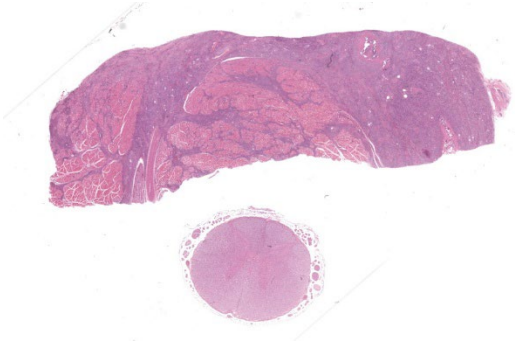
Microscopic Description:
Right cervical mass: Surrounding and extending within the skeletal muscle there are extensive areas of fibrous connective tissue containing large numbers of epithelioid macrophages, lymphocytes, plasma cells and few neutrophils, as well as frequent fibroblasts. Within the fibrous tissue, there are multifocal areas of necrosis often centred on well-defined round clear spaces (lipid or oil), and these foci are surrounded by epithelioid macrophages with giant cell formation. Necrotic areas often display mineralization and occasionally contain aggregates of acid-fast rod-shaped organisms. Adjacent to granulomatous inflammation there are numerous hypereosinophilic myofibres which are often small and angular, and

sometimes display centralized nuclei (degeneration and atrophy). Occasional myofibres contain protozoal bradycysts (consistent with Sarcocystis spp.).

Spinal cord: Within the white matter of the ventral and lateral funiculi there is frequent swelling of myelin sheaths which often contain degenerate gitter cells (digestion chambers). There are also enlarged astrocytes scattered throughout the white matter in these areas.

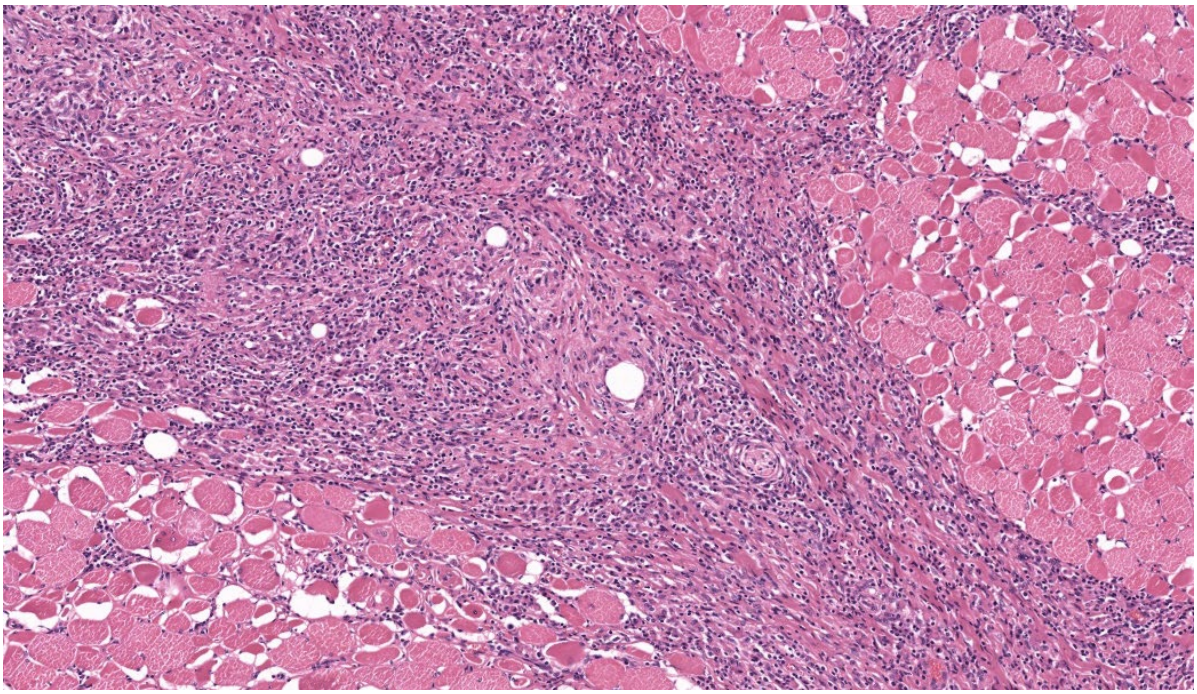
Contributor's Morphologic Diagnosis:
Cervical musculature: granulomatous perimyositis, chronic, diffuse, severe with intralesional acid-fast material, marked fibrosis and moderate myofibre degeneration and atrophy
Cervical spinal cord: Degenerative axonopathy, chronic, regional, moderate

Contributor's Comment:
The submitted case is an example of vaccine-induced compressive myelopathy secondary to injection with *Mycobacterium avium* subsp. paratuberculosis vaccine (Gudair - imported from CZ Veterinaria, Porrino, Spain by Pfizer Animal Health). Gudair is a killed vaccine containing whole bacteria, paraffin oil, and thiomersal, and is indicated for single-dose subcutaneous injection behind the ear. Granuloma formation is a well-recognized side-effect of vaccine administration, both within the subcutis and also within the underlying cervical musculature if the vaccine is inadvertently delivered into the deeper tissue[2,4-5,6,8-9]. After introduction of the Gudair vaccine to Australia in 1999, a field trial was undertaken by L. Reddacliff et. al. from 1999 to 2004 on 1200 lambs aged 1-3 months on 3 farms in the central tablelands of New South Wales[5]. Reddacliff et al. observed that at 2 months post-vaccination, 42% of the vaccinated lambs had nodular vaccine site lesions with a diameter ranging from 3-45 mm[3]. Only 20 % of the vaccinated lambs had palpable vaccine site lesions by 3-4 years of age, interestingly with no decline in the average diameter of the nodules. Histologically, these lesions were described as multifocal to coalescing necrotizing granulomatous dermatitis and cellulitis[4,5]. Intralesional mycobacteria, representing residual killed vaccine organisms, were observed in 87.5 % of cases, but these did not grow in aerobic or anaerobic cultures [4,5]



3-2. Skeletal muscle and cervical spinal cord, sheep: One section each of the skeletal muuscle and cervical spinal cord are submitted.. At subgross magnification, there is a marked cellular infiltrate infitlrating along the epimysium and perimysium of the skeletal muscle. (HE, 7X)

Consistent with previous reports, we observed well-defined round clear spaces associated with necrotic areas[2]. These clear spaces represent the lipid or oil base that acts as the adjuvant of the Gudair vaccine[2]. Although the mechanism of action of oil is not fully described, it is thought to trap the antigen at the site and release it over an extended period, prolonging immune stimulation. The Gudair vaccine composition of mycobacteria combined with oil essentially mimics Freund's adjuvant, a substance shown to induce potent cellular immunity that also leads to granulomatous inflammation in different tissues. Granulomatous inflammation is also induced by the oil fraction alone but to a lesser degree compared to the full vaccine[3].



3-3. Skeletal muscle, sheep: The cellular infiltrate expanding the perimysium is composed of abundant epithelioid macrophages admixed with fewer lymphocytes and plasma cells, plump fibroblasts, and fibrosis. There are clear vacuoles scattered throughout the infiltrate and mild atrophy of adjacent myocytes. (HE, 187X)

Extension of the Gudair vaccine site reactions or granulomatous lesions into the cervical spinal canal has been reported previously[6,7]. In these reports, incorrect administration of the vaccine induced the formation of a smooth mass protruding dorsally into the cervical spinal cord at the level of C1-C2. Histologically, the cases displayed features of compressive myelopathy, with variable grey matter neuropil necrosis, hemorrhage, Wallerian degeneration of all funiculi, and glia cell infiltration[6]. These findings demonstrate that incorrect administration of Gudair vaccine intramuscularly or adjacent to the vertebrae may lead to spinal cord compression due to local granulomatous inflammation.

We received 3 more lambs aged 3-5 months from the same farm with the same clinical history. All lambs had similar gross and histopathological findings to those present in the submitted case, including granulomatous inflammation within the lateral subcutaneous and cervical musculature. We also observed well-demarcated clear spaces (presumably oil) associated with necrotic areas within the granulomatous inflammation in cervical musculature and scant bacteria in some areas of necrosis in all the lambs. The neurological issues ceased following training of staff in correct vaccine administration.

Contributing Institution:
Veterinary Anatomic Pathology, Faculty of Veterinary and Agricultural Sciences, The University of Melbourne
https://www.u-vet.com.au/

JPC Morphologic Diagnosis:

1. Skeletal muscle: Myositis , granulomatous and necrotizing , chronic, multifocal to coalescing, marked with lipid vacuoles.

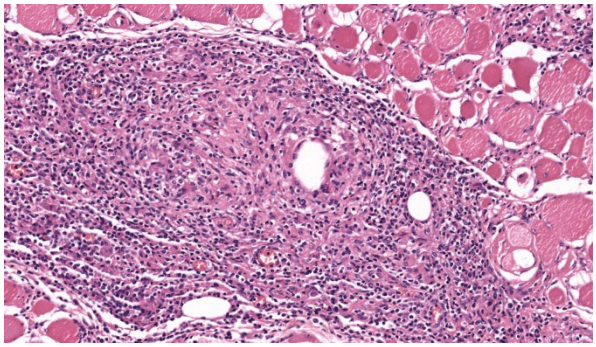
2. Spinal nerve root, epineurium: Radiculoneuritis, granulomatous and lymphoplasmacytic, chronic, diffuse, moderate.

3. Spinal cord, lateral and ventral funiculi: Axonal degeneration, multifocal, mild.

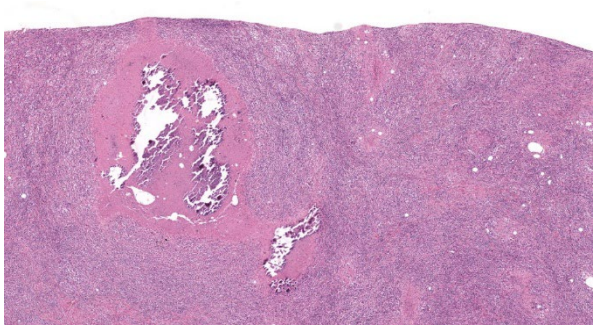
4. Skeletal muscle: Sarcocysts, multiple.

JPC Comment:

The contributor has provided an excellent review of the Gudair vaccine, which is making its debut in the Wednesday Slide Conference. However, the effects of oil-based vaccines are not new to the Wednesday Slide Conference. In the last decade, two WSC cases have involved compressive myelopathy resulting from vaccination of cattle with oil-in-water adjuvanted vaccines against foot-and-mouth disease, a common practice in South America. In both cases, injection of an oil-in-water adjuvanted vaccine extended from a muscle abscess/granuloma through the spinal foramina into the spinal canal, compressing the spinal cord. Typically, these myelopathies affect the white matter, resulting in Wallerian degeneration of axons, while leaving the grey matter



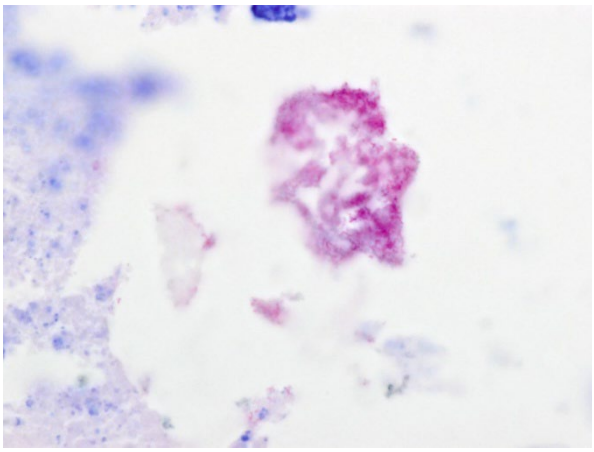
3-4. Skeletal muscle, sheep: High magnification of the inflammatory infiltrate surrounding clear foci of presumptive vaccine material. (HE, 381X)



3-5. Skeletal muscle, sheep: There are geographic areas of lytic necrosis with mineralization within the inflammatory exudate. (HE, 381X)

unscathed.[10] (This is typical of chronic compression, whereas acute compression typically affects the grey matter.)[10] The paresis and paralysis seen in affected animals may not only be the result of spinal cord compression, but also of the spinal nerve roots as well, whose thin root sheath and scant endoneurial collagen make them easily compressed by advancing inflammation.[10] (This is typical of chronic compression, whereas acute compression typically

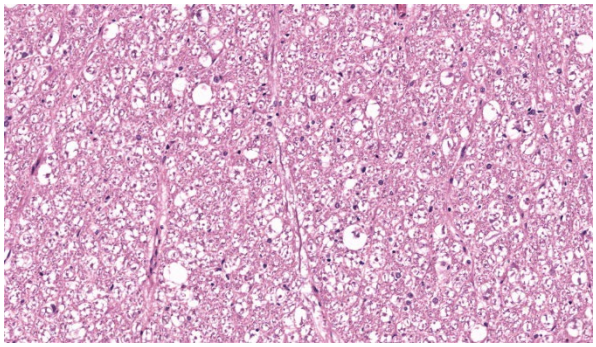
A 2019 article by Asin *et al.*[11] further explores the use of oil-in-water adjuvanted vaccines in small ruminants, documenting the gross lesions, histopathology, and ultrastructure of the granulomas that they cause, as well as briefly describing a systemic autoimmune disease in a subset of vaccinated animals referred to as ovine ASIA (autoimmune/systemic inflammation induced by adjuvants) syndrome. Ovine ASIA syndrome has a significant adverse effect on sheep production following widespread bluetongue vaccination in the late 2010s. Like the oil-in-water vaccines used to vaccinate cattle against FMD, aluminum salts are used as the adjuvant and, while potentiating the vaccine's antigenic effects, also likely result in granuloma/abscess formation and systemic inflammation in sheep, which are very susceptible to these effects. (In cattle, the



3-6. Skeletal muscle, sheep: There are rare aggregates of acid-fast rods within areas of lytic necrosis. (*Photo courtesy of:* Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, https://www.u-vet.com.au/). (Ziehl-Niehlsen, 600X)

highest frequency of granulomas is seen in oil-in-water bacterins, prompting the supposition that endotoxins released from dying bacteria may potentiate tissue damage at the site of vaccination.)[10]

Ovine ASIA syndrome, as previously stated, was first described following a widespread bluetongue vaccination campaign in the late 2010s. ASIA has both an acute and chronic phase, and in this study, it was reproduced following repeated vaccinations with aluminum-adjuvanted oil-in-water vaccines. The acute phase, which appears 2-6 days following inoculation, results in acute meningoencephalitis and diminished response to external stimuli. The less common (or at least less commonly observed) acute phase appears 2-6 days after an adjuvant-containing inoculation. An acute neurological episode with low response to external stimuli and a high rate of recovery characterizes it. Most animals apparently recover afterward. The chronic phase is seen in a higher proportion of flocks. The chronic phase, seen in a higher percentage of flocks, begins with an excitatory phase, often triggered by low temperatures, and is followed by weakness, extreme cachexia, tetraplegia, and death. The cachexia is characterized by severe muscular atrophy, and microscopic lesions are mostly linked to a neurodegenerative process in both dorsal and ventral columns of the gray matter of the spinal cord. Experimental reproduction of ovine ASIA in a small group of repeatedly vaccinated animals was successful.[12]



3-7. Spinal cord, sheep: Lateral and ventral funiculi contain low numbers of dilated myelin sheaths with axonal debris or Gitter cells within them. (HE, 385X)

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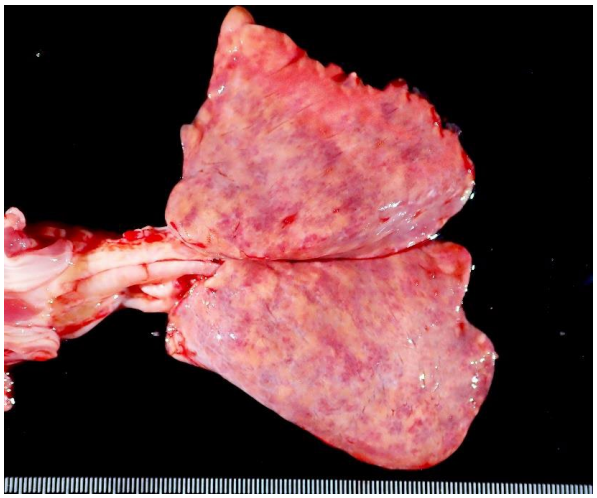
CASE IV:

Signalment:
A 1-year-old female northwest Bornean orangutan (*Pongo pygmaeus*)

History:
Uneventful clinical history, raised within a family group of orangutans. Without any prior clinical signs, on 22nd May she was found in a semi-comatose state with little muscle tone and carried alternately by different females. She became less responsive and died before veterinary assistance could be provided.

Gross Pathology:
Several subacute to chronic superficial mild wounds on the forehead and face. Within the left hemithorax there is approximately 20 mL of free sero-sanguinolent fluid. Both lungs appear consolidated and present randomly distributed multifocal to coalescing dark red and yellowish patches.



4-1. Lung, orangutan: Diffusely, alll lung lobes have multifocal to coalescing yellow to red, variably sized foci (*Photo courtesy of:* Department of Animal Health and Anatomy, Autonomous University of Barcelona).

Laboratory Results:
All the previous routine group coprological tests (stool test and cytology) were negative.

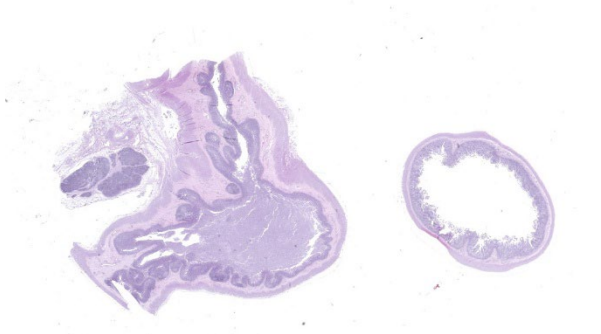
Blood drawn shortly post-mortem showed severe, normocytic, normochromic anemia with marked anisocytosis and slight anisochromia.

No significant bacterial or fungal pathogen was isolated from the lung sample.

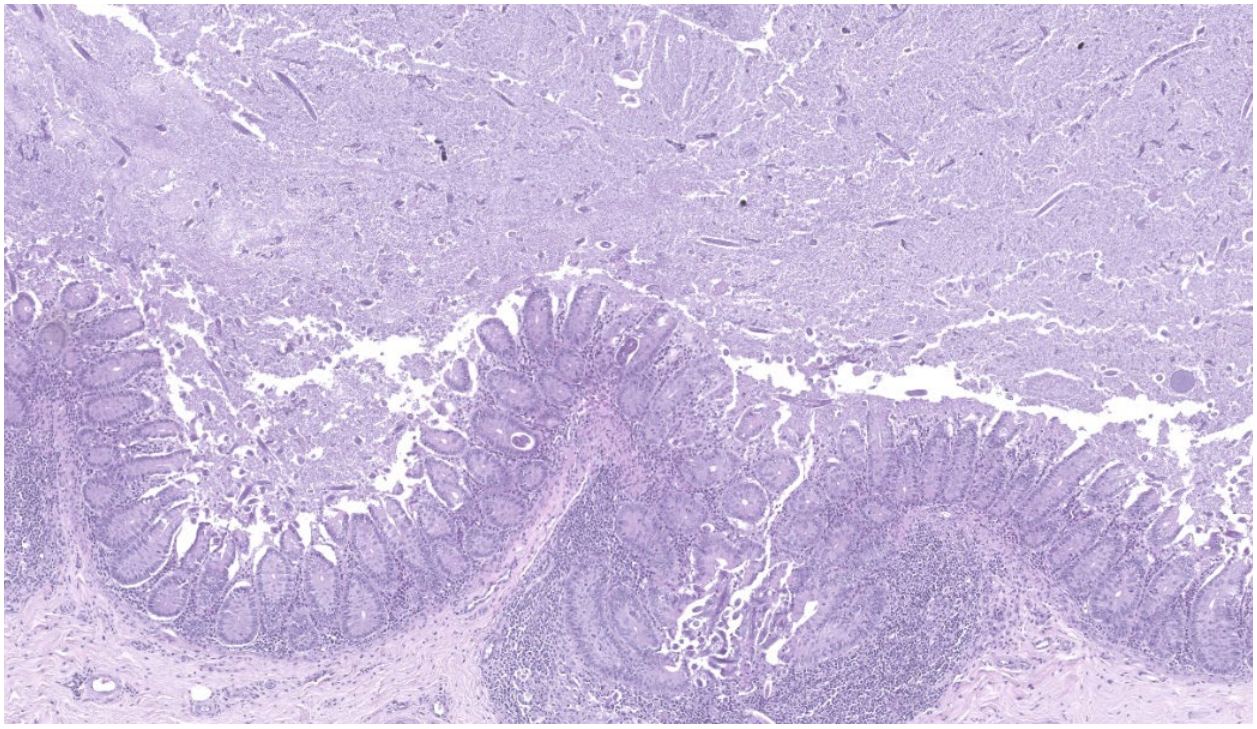
Microscopic Description:
Ileum (ileocecal valve): effacing 80% of the sample there is a subacute, moderate, inflammatory, and necrotizing process mainly localized in the mucosa of the ileocecal valve. There are multifocal areas of moderate to severe erosions with loss of the mucosa, intraluminal neutrophils, hemorrhages, and bacterial colonies. Intralesional, slender adult nematodes are observed. They are in the lumen of the glands, they have 40-50 um length, 2-3 um width, external thin cuticle, hypodermis, pseudocelomen with platymiarian musculature, digestive tract with uninucleate cells and paired genital tract that contain uninucleate eggs. Occasionally ovoid to rounded, eosinophilic eggs 30-50 µm in diameter appear within the epithelium of the mucosa. In the lamina propria macrophages, lymphocytes, plasma cells and low numbers of eosinophils. There is also moderate hyperplasia of intestinal glands.

Cecum and regional lymph node: diffusely, the whole section of the cecum shows a diffuse, subacute, moderate inflammatory process that affects mucosa and submucosa. The lumen of the cecum is filled with debris, coccoid bacterial colonies, and high number of nematode larvae (cross and longitudinal sections), that also appear in the lumen of the intestinal glands. Most of the larvae are 200-300 µm in length, 16 µm width and present a small buccal capsule, rhabditid large esophagus, prominent genital primordium, and straight tail (rhabditiform larvae). There is also another type of larvae, they are larger and thinner, measuring 630 µm and 16 µm (filariform larvae), present in the lumen and invading the mucosa. In the lamina propria, there is a diffuse, moderate inflammation composed of lymphocytes and plasma cells, with multifocal areas of eosinophilic and neutrophilic infiltration. Multifocally, there are numerous filariform larvae in the submucosa with only occasional inflammatory reaction. The GALT is active with slight increased numbers of histiocytes in the germinal centers. Additionally, there is mild dilation of lymphatic vessels, both in the serosa of the intestine and in the lymph node capsule, some of them containing intraluminal bacteria (GRAM positive) and very occasional larvae (cross section). In the lymph node there is mild presence of eosinophils.

Lung (not submitted): all the evaluated section showed a marked widening of the alveolar septa due to hyperplasia and hypertrophy of type II pneumocytes and increased number of mononuclear inflammatory cells in the interstitium. Alveolar lumen was filled with high numbers of foamy macrophages that contain



4-2. Ileocecal junction and cecum, orangutan: A section of ileocecal junction (left) and cecum (right) are submitted for examination. At this low magnification, the innumerable mixed bacterial within the lumen of the ileocecal junction are evident. (HE, 7X).



4-3. Ileocecal junction, orangutan: Large numbers of larval and adult rhabditid nematodes are present within the lumen and crypts of this section of gut. Cross sections of adult nematodes are present within crypt epithelial cells. There are innumerable bacteria within the lumen. (HE, 113X).

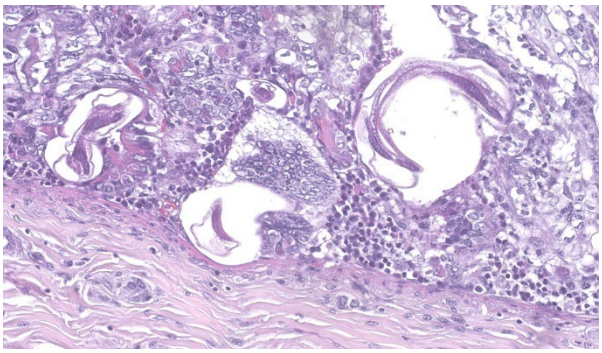
brown intracytoplasmic granules (hemosiderophages) associated with multifocal areas of extravasated erythrocytes (hemorrhage). Multifocally and admixed with the hemorrhage there is moderate numbers of small fibrin thrombi in small blood vessels (DIC). Intraluminal nematode larvae are observed in small blood vessel.

Contributor's Morphologic Diagnoses:
Ileum (ileocecal valve): multifocal to diffuse, subacute, moderate, necrotizing, lymphohystiocytic and eosinophilic ileitis with intralesional eggs and adult female nematodes (Strongyloid spp)

Cecum: multifocal to diffuse, subacute, moderate, necrotizing, lymphohystiocytic and eosinophilic typhlitis with massive strongyloid larvae (rhabditiform, L1 and filariform, L3) infestation.

Lung: severe, generalized fibrino-haemorrhagic and granulomatous pneumonia with intralesional Strongyloid larvae

Contributor's Comment:
The present case was an example of a hyperinfection in a young orangutan by *Strongyloides spp*. with systemic dissemination. The lesions observed in the lung were severe, and the presence of DIC in alveolar capillaries suggested that the animal suffered septic shock, probably due to bacteria accompanying larval migration. Although the intestinal parasitic load was high, macroscopic lesions were exclusively in the lungs, which is in accordance with the revised bibliography. Environmental factors may have played a role in this case, as the mother showed relaxed maternal behavior, allowing other females to tend to the youngsters, and the group had space restrictions due to construction work. Parasitological examinations of the group, both before and after this



4-4. Cecum, orangutan: Cross sections of adult rhabditid nematodes are present within crypts and often with crypt epithelial cells. (HE, 574X)

incident, have been negative by Baermann's sedimentation (10+ samplings, tested in-house and at an outside lab).

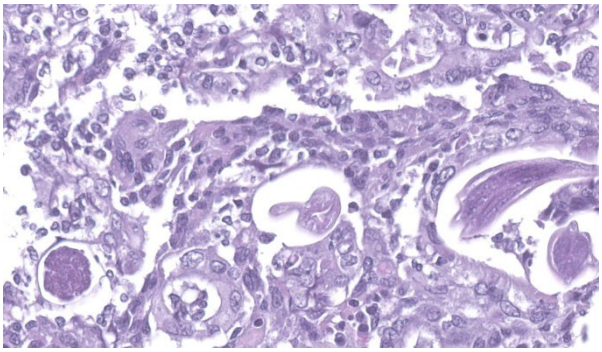
Strongyloides is a genus of small nematodes belonging to the order Rhabditidia. Other common genera in this group include *Rhabdias*, *Pelodera* and *Halicephalobus*. These worms have platymyarian musculature and an intestine composed of uninucleate cells, and *Strongyloides* spp. are characterized by paired genitalia.[3]

Strongyloides nematodes affect millions of people worldwide and have been reported in all great ape species and some Old World primates.[5] Of the great apes, orangutans ≤5 years old appear to be the most susceptible to severe clinical disease, likely due to their immunologically naïve status.[5] Infections can be fatal and may represent a major cause of death in captive individuals.[11]

Most infected animals and humans are asymptomatic shedders, and *Strongyloides* eggs or larvae are frequently identified in coprological studies of apes in captivity and in the wild.[2] Two species can parasitize hominids: *Strongyloides fuelleborni* (OW monkeys and apes are natural hosts) and *S. stercoralis* (human natural hosts).[7] *Strongyloides stercoralis* is primarily a human parasite in the Southern Hemisphere, but infections have occasionally also been described in non-human primates, causing severe disease or death.[6] *S. fuelleborni* is found in monkeys and apes in Africa and Asia and comprises two subspecies: *S. fuelleborni fuelleborni* and *S. fuelleborni Kelly*. Human infections with this subspecies occur sporadically in Africa.[9]

Infection occurs by percutaneous penetration or ingestion of third-stage filariform larvae.[10] L3 then enter the circulation and travel through the heart to the lungs, where they undergo further development in alveoli. Developing larvae are then coughed up, swallowed, and penetrate the wall of the small intestine, where they develop into parthenogenic adult females that live in the crypts and produce eggs that are shed in the feces (*S. fuelleborni*) or hatch in the lumen to release larvae that are shed in the feces (*S. stercoralis*)[7]. Environmental L1 can develop directly into infectious L3 larvae, or into free-living adult males or females which produce eggs and larvae by sexual reproduction. Likewise, their progeny may either develop into new generations of infectious L3 larvae or noninfectious free-living adults.[10]

Diagnosis based on coproscopy can be challenging, as it requires Baermann's sedimenta-



4-5. Cecum, orangutan: Cross sections of adult rhabditid nematodes demonstrate a triradiate esophagus. (HE, 680X)

tion (funnel technique). In contrast, the flotation technique does not reliably detect the L1.[1] Treatment options for *Strongyloides* infection include azole drugs and ivermectin.[5]

Recommended control measures include maintaining exemplary exhibit hygiene and utilization of Baermann or formalin-concentrating fecal screening techniques to identify and treat subclinical infections in all orangutans.[5] Crowding, ground dwelling, and bad hygiene, which may occur in populations of captive orangutans, can cause constant reinfection, especially with *Strongyloides stercoralis.*[8] It is therefore important to avoid high densities of animals in the facility if possible. In 2020, the Association of Zoos and Aquariums (ASP) within the "Orangutan Species Survival Plan (SSP)" elaborated a review and recommendations for Strongyloides infection in orangutans, which proposed the prophylactic use of ivermectin in case of clinical suspicion.

Orangutans (*Pongo* spp.) are threatened in their survival due to habitat loss, hunting, and infections such as Strongyloidiasis, which may represent a severe cause of death in wild and captive individuals.[6]

Regarding non-primate hosts, *S. stercolaris* infects cats and dogs, and it has also been reported in arctic foxes.[4] Other relevant species are *S. papillosus* in ruminants, *S. westerii* in horses, *S. ransoomi* in swine, and S. felis, S. planiceps, and *S. tumefaciens* in cats.[3]

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JPC Diagnosis:
Ileocecal junction: Enterotyphlitis, necrotizing, subacute, diffuse, moderate with adult and larval rhabditid nematodes and eggs.

JPC Comment:
The contributor has produced an excellent review of *Strongyloides stercoralis* in veterinary species, and it parallels the pathogenesis in humans quite closely. One review of 31 isolates of Strongyloides sp. in Bornean orangutans (and one keeper) speciated 30/31 as *S. fulleborni,* with only one speciated as S. stercoralis.[6]

Both rhabditiform and filariform larvae may infect the host via ingestion. Still, only filariform larvae may infect the host via skin penetration (Urocanic acid, a histidine metabolite present in high concentration in the skin of mammals, appears to be a potent chemoattractant.)[13] Following tissue migration (most commonly in the lungs), filariform larvae become adults in the proximal small intestine, where adult females lay eggs which hatch into rhabditiform larvae. These larvae may be shed in the stool, completing the sexual cycle, or may transform into filariform larvae, which, after exiting and re-entering the gut, may result in reinfection (aka *autoinfection*). Multiple cycles of autoinfection result in *hyperinfection*.

Rarely, and most often associated with immunosuppression, *Strongyloides stercoralis* may leave its favored locations in the body (skin, gut, and lung), resulting in disseminated infection that may be fatal. Because CD4+ TH2 lymphocytes are the primary driver of immunity to S. stercoralis infection, it stands to reason that drugs or diseases that cause immunosuppression (HTLV-1, malnutrition, alcoholism, among others) will promote hyperinfection or disseminated infection.

While Strongyloides sp. in most domestic species involves the proximal small intestinal mu-

cosa, in a few mammalian species, the nematode parasitizes other segments of the GI tract. In macropods, *Strongyloides* infects the gastric mucosa, particularly in the cardiac region. In cats, a particularly interesting manifestation is seen (WSC 2021-2022, Conference 6, Case 1) in which invasion of the colonic mucosa by adult females results in the formation of proliferative nodules of colonic epithelium within the colonic submucosa. The *Strongyloides* sp. observed within feline colonic nodules was designated as a separate species, *Strongyloides tumefaciens*, by the authors who first described it in 1927.[13] The species designation was based primarily on the unusual location and lesion, rather than on nematode morphology. Thus, the validity of this species is questionable, and a molecular genetic approach to this parasite's identification would seem warranted.

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